

ABSTRACT

Novel drug complexes comprising a polypeptide carrier moiety comprising glutamic acid and at least one of the group consisting of aspartic acid, alanine, asparagine, glutamine, glycine, and any combinations thereof, are disclosed. The drug moiety is a therapeutic metal selected from the group consisting of platinum, iron, gadolinium, rhenium, manganese, cobalt, indium, gallium or rhodium. Methods for making said complexes, compositions comprising said complexes, methods for making saiduch compositions, and methods for treating a patient comprising use of said complexes and/or compositions are further disclosed.

Mol Percent Report

Sample ID: 01402018 (initiated 1/15/99 7:03am) BASELINE CORRECTED

Turntable Position: 6 C Sampling Interval: 1.0 sec
 Data Start : 3.00 min Samples In Run : 72
 Data Duration : 16.00 min Operator ID :
 Peak Ht Threshold : 3000 uAU Int. Std. Amt : 250 pmol

Calibration File : 14JANCAL (initiated 1/15/99 9:44am)
 Reference Time : 0.00 min (No ISTD Peak Specified)
 Reference Offset 1: -0.02 min
 Reference Offset 2: 0.00 min

Integration Interval: 0.0 to 16.0 min

PEAK ID	RET. TIME min	PMOL BY HEIGHT	PMOL correc. INT STD	MOL %
ASX	2.30	562.99	0.00	29.02
GLX	2.70	1377.05	0.00	70.98

TOTAL PMOLS RECOVERED 1940.04

Minimum Peak Threshold: 3000 uAU (53 peaks below threshold)
 (8 peaks found)
 (2 peaks matched)

Figure 1B.

Amino acid analysis of the polypeptide

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 Metal Complexes and Compositions, Methods of Making, and
 Methods of Using Same"

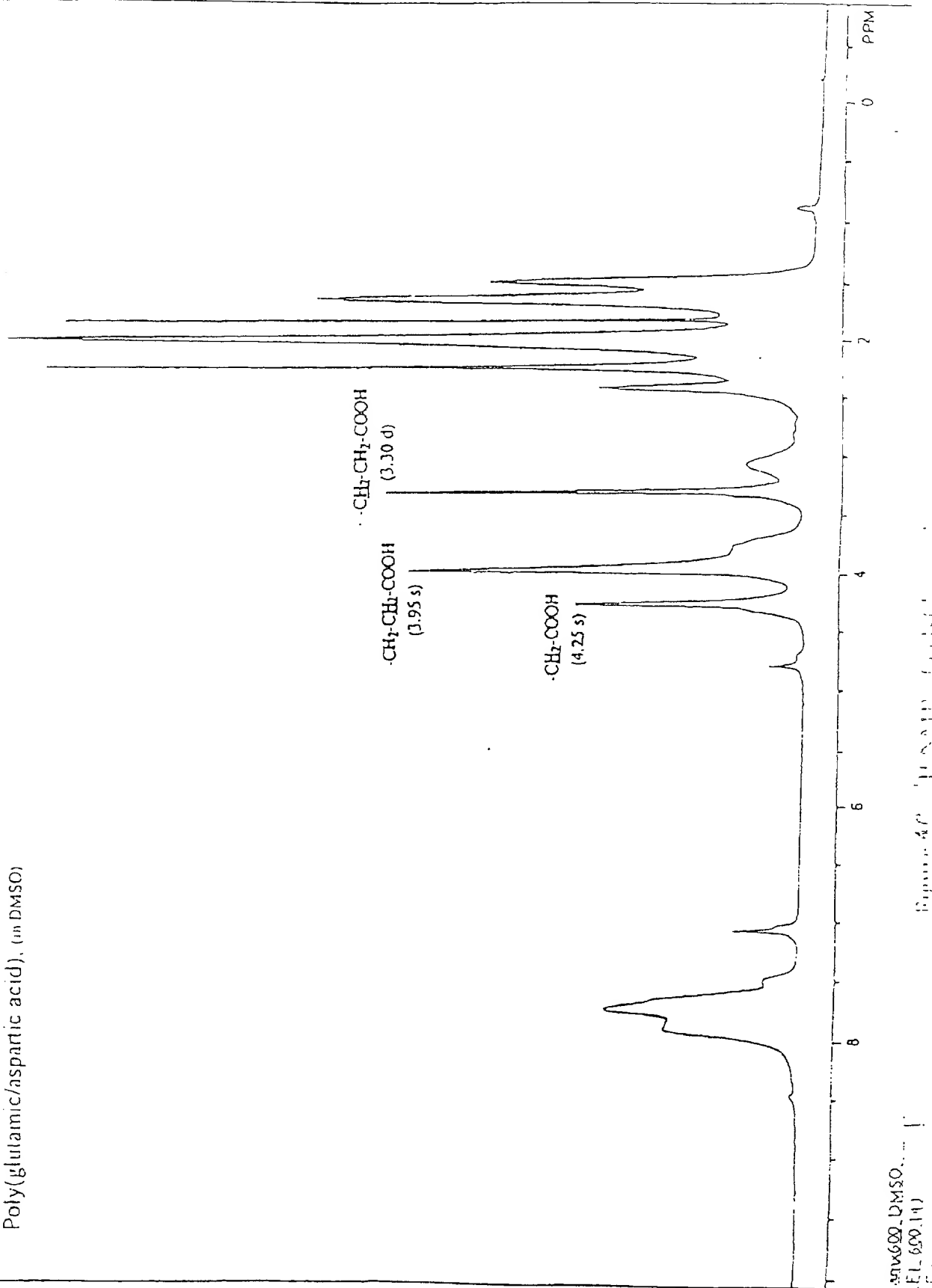
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102280-08F04650

Poly(glutamic/aspartic acid), (in DMSO)



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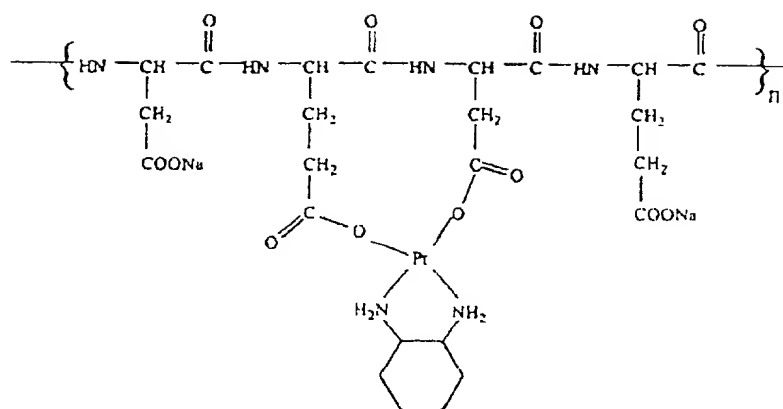
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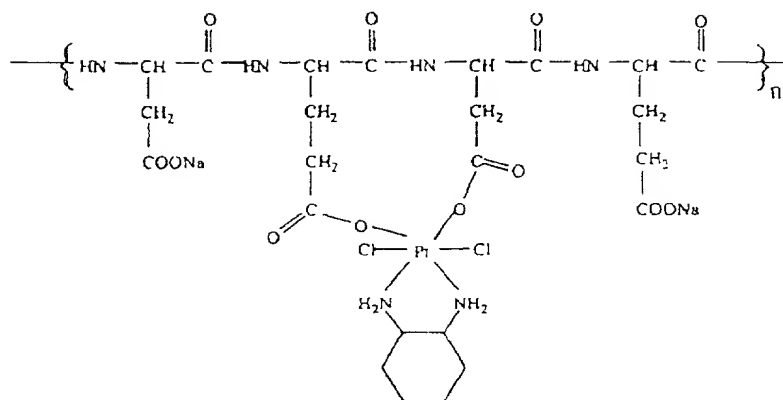
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00440460 0370460



Pt(II) Complex



Pt(IV) Complex

Figure 2.

Structures of platinum(II) and platinum(IV)-poly(dipeptide) complexes



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LABORATORY REPORT

SAMPLE ID	LAB ID	ANALYSIS	RESULT(S)
DACH	I-5746	Platinum	44.60 %
PPAP	I-5747	Platinum	16.11 %
PDDP	I-5748	Platinum	17.64 %

Figure 10

Elemental analysis of platinum-poly(dipeptide) complexes for Pt(II)(PDDP), Pt(IV)(PPAP) and cis-1,2-DACH-Pt SO₄(DACH)

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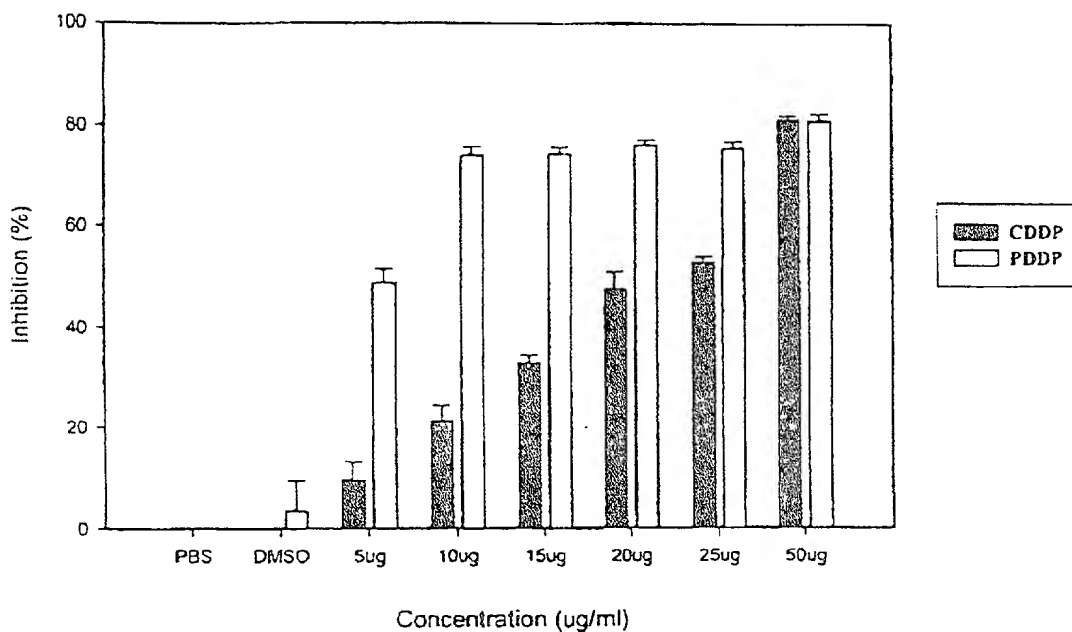
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Effect of PDDP & CDDP on Inhibition of Human Sarcoma Cells (HT1080) at 48 Hours



Effect of PDDP & CDDP on Inhibition of Human Sarcoma Cells (HT1080) at 72 Hours

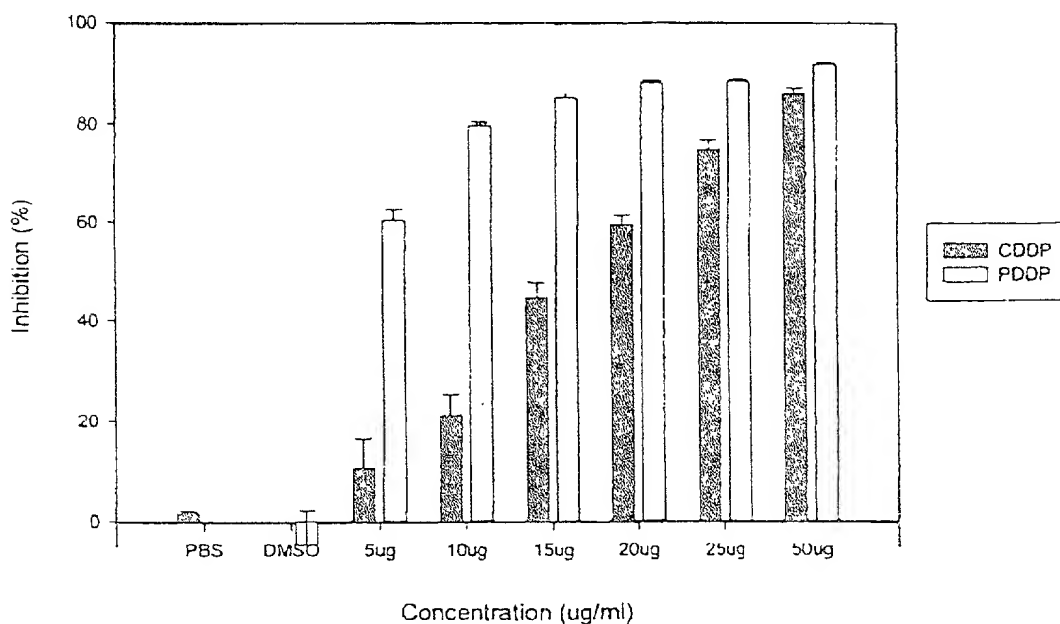


Figure 4A

In vitro cell culture assay of cisplatin(CDDP) and poly(glutamate/aspartate) acid-1,2-DACH-Pt(II) complex(PDDP) in human sarcoma

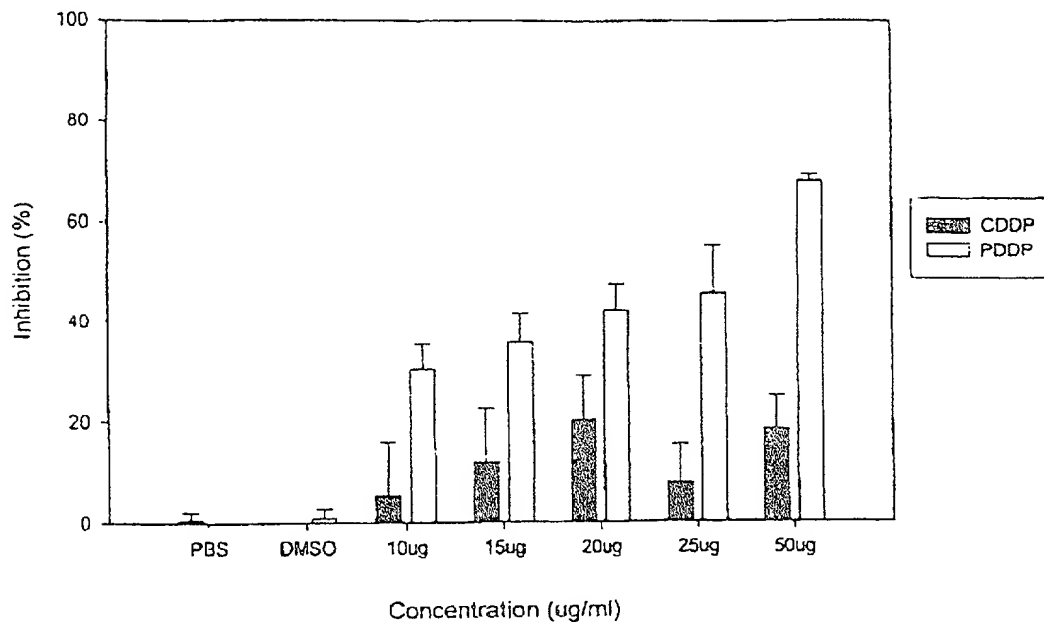
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Effect of PDDP & CDDP on Inhibition of Human Prostate Cancer Cells (A10) at 48 Hours



Effect of PDDP & CDDP on Inhibition of Human Prostate Cancer Cells (A10) at 96 Hours

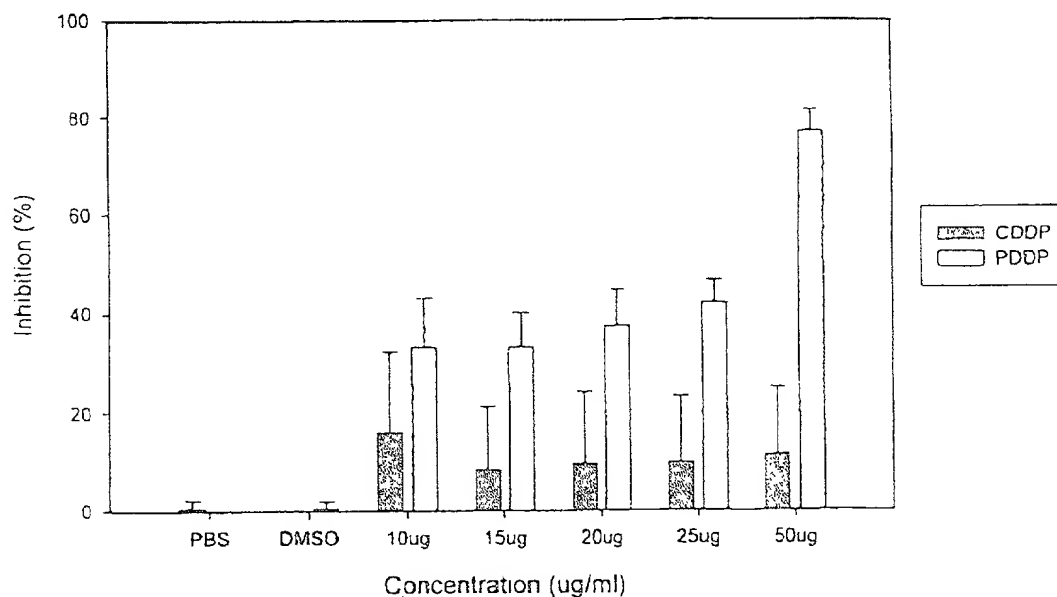


Figure 4-B

In vitro cell culture assay of cisplatin(CDDP) and poly(glutamate/aspartate) acid-1,2-DACH-Pt(II) complex(PDDP) in human prostate cancer

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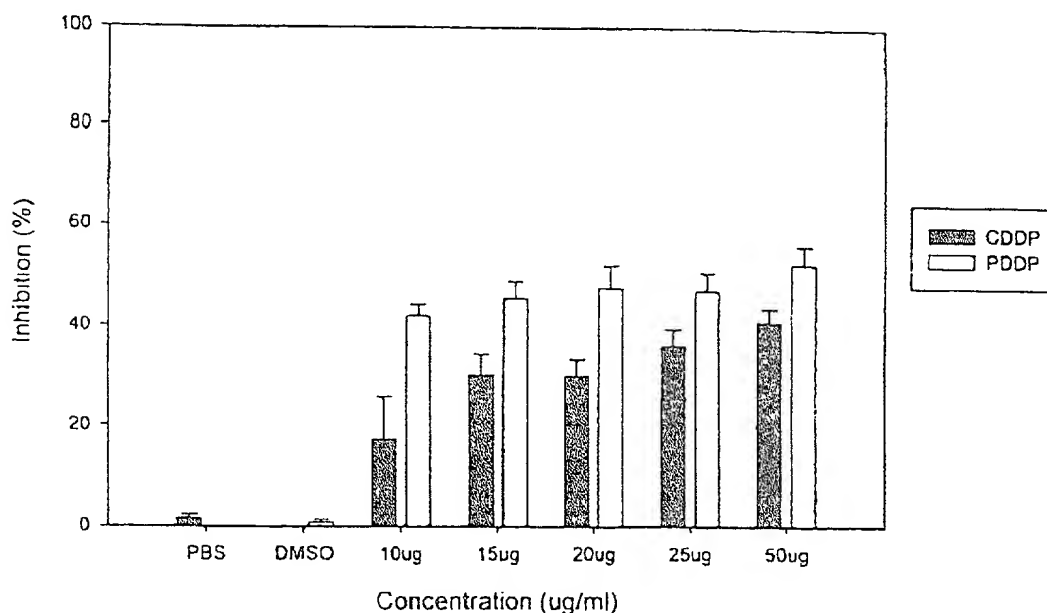
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Effect of PDDP & CDDP on Inhibition of Human Prostate Cancer Cells (PC3) at 48 Hours



Effect of PDDP & CDDP on Inhibition of Human Prostate Cancer Cells (PC3) at 96 Hours

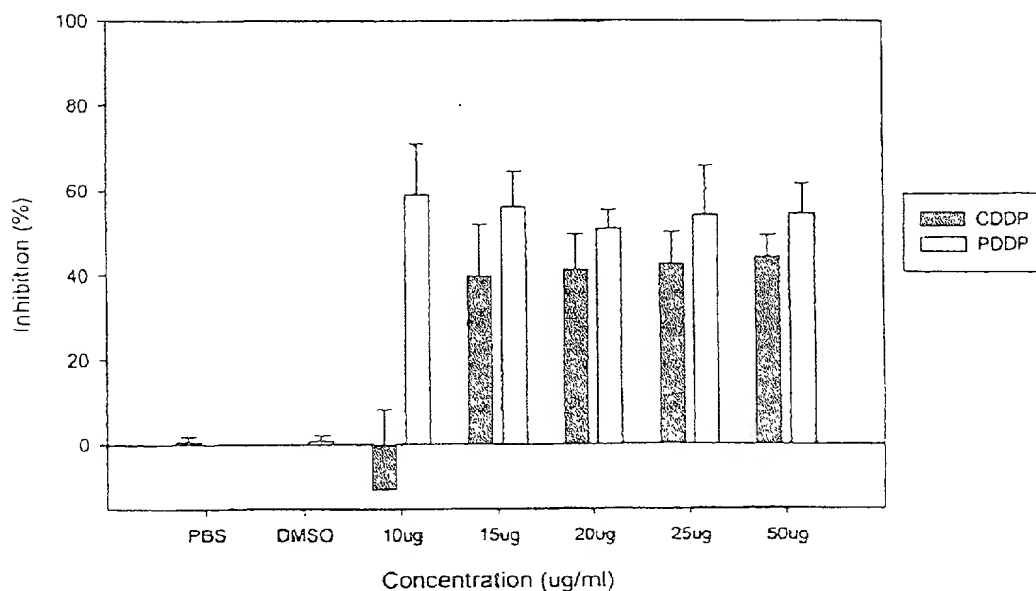


Figure 5C

In vitro cell culture assay of cisplatin(CDDP) and poly(glutamate/aspartate) acid-1,2-DACH-Pt(II) complex(PDDP) in human prostate cancer

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Anti-tumor Activity of PDDP Against Rats Bearing Breast Tumors (13762)

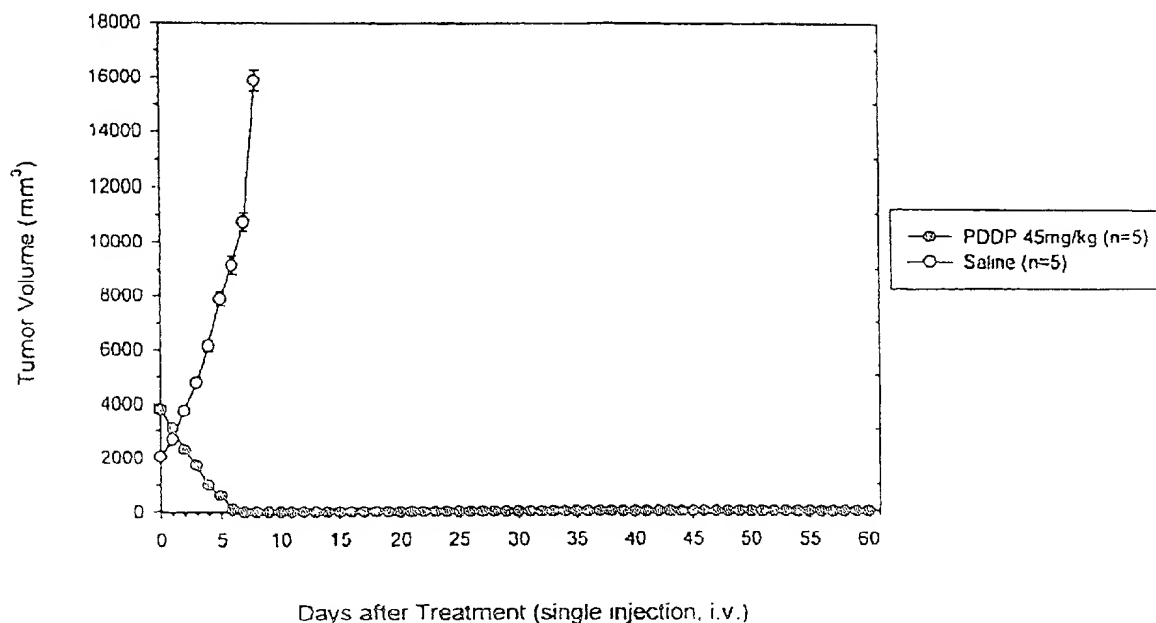


Figure 5

In vivo anti-tumor activity of an inventive poly(glutamate/aspartate) acid-1,2-DACH-Pt(II) complex (PDDP) compared to control against rats bearing breast tumors.

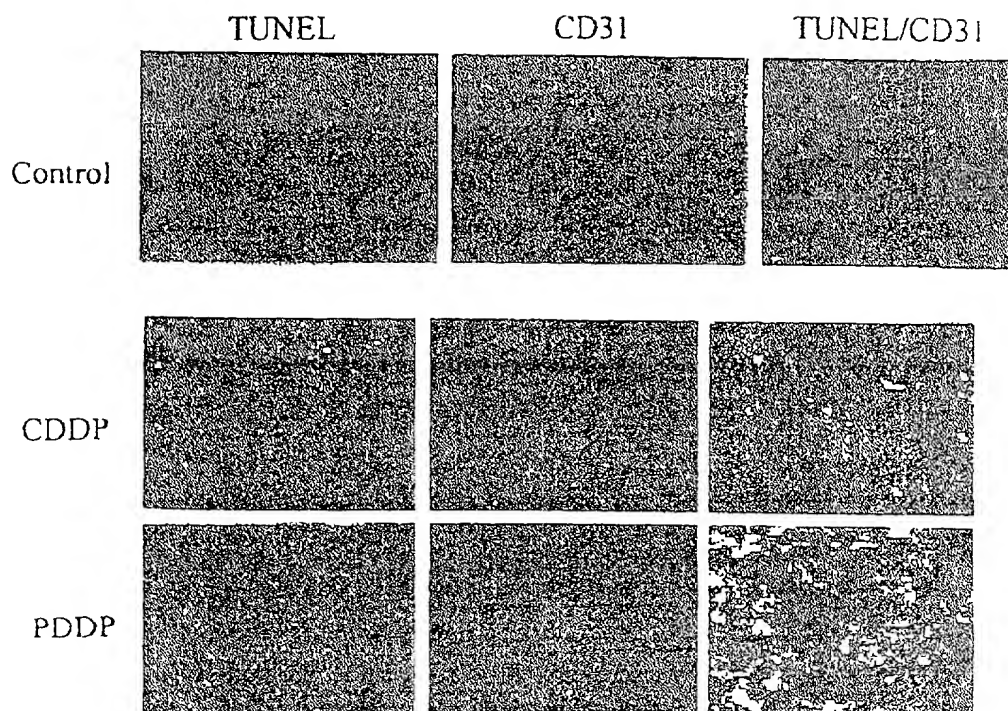


Figure 5

The specific cellular target expression changes at 48 hours post treatment of poly(glutamate/aspartate) acid-1,2-DACH-Pt(II) complex (PDDP), cisplatin (CDDP) and saline (control)

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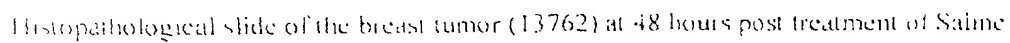
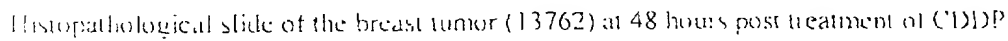
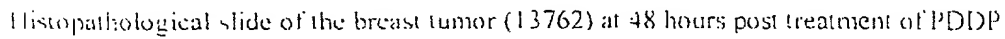


Figure 7

The histopathological changes of breast tumors (13762) at 48 hours post treatment of poly (glutamate/aspartate) acid-1,2-10AC11-Pt(II) complex (PDDP), cisplatin (CDDP) and Saline